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Anterior Approach for Major Right Hepatic Resection for Large Hepatocellular Carcinoma

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Objective
To report the surgical and long-term outcomes of major right hepatic resection for large hepatocellular carcinoma (HCC) using the anterior approach compared with the conventional approach.

Summary Background Data
Great difficulty can be encountered during major right hepatic resection for large HCC using the conventional approach. Forceful retraction during mobilization of the tumor might result in serious complications, including dissemination of cancer cells, iatrogenic tumor rupture, and excessive bleeding, leading to unfavorable surgical and long-term outcomes.

Methods
In patients who had large HCC at the right lobe of liver and underwent major hepatic resection, the technique of anterior approach was used. After hilar control of the inflow blood vessels and without prior mobilization of the right lobe of liver and the tumor, parenchymal transection was performed using an ultrasonic dissector from the anterior surface of the liver until the anterior surface of the inferior vena cava was exposed. All venous tributaries, including the right hepatic vein, were controlled before the right lobe of liver was mobilized. Surgical and long-term outcomes were analyzed retrospectively and compared with patients who underwent surgery using the conventional approach.

Results
From 1989 to 1997, the anterior approach was used for major right hepatic resection in 54 patients with HCC of 5 cm or more in diameter. When compared with the 106 patients with similar clinical parameters who underwent hepatic resection using the conventional approach during the same period, the patients in the anterior approach group had significantly less intraoperative blood loss and blood transfusion, a lower hospital death rate, a lower incidence of pulmonary metastases, and a better median disease-free survival and median overall cumulative survival.

Conclusion
The anterior approach is the preferred technique for major right hepatic resection for large HCC because it resulted in improved surgical and survival outcomes compared with the conventional approach.

During right hepatic resection for hepatocellular carcinoma (HCC), complete mobilization of the right lobe of liver with the right hepatic vein controlled outside the liver before parenchymal transection has been advised by most surgeons,[1–4] and this conventional approach has been suggested to be helpful in reducing the amount of surgical blood loss.[5] However, the conventional approach may not be feasible in some patients with large HCC undergoing major right hepatic resection. The tumor may infiltrate into the surrounding structures, and the size of the tumor may limit access to the posterior aspect of the right lobe of liver and the anterior surface of the inferior vena cava, where the right hepatic vein and many caval branches are present. Injudicious mobilization of the liver may carry theoretical risks of excessive bleeding from avulsion of the hepatic vein and caval branches, prolonged ischemia of the liver remnant from rotation of the hepatoduodenal ligament,[6] iatrogenic tumor rupture, and spillage of cancer cells into the systemic circulation. Alternatively, the anterior approach can be adopted for patients requiring difficult major right hepatic resection for HCC. The technique involves initial completion of parenchymal transection before the right lobe is

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mobilized. Our initial experience of the anterior approach in a heterogeneous group of patients with large right-lobe liver tumors, including benign and malignant ones, showed that it was a safe and effective option for selected patients undergoing major right hepatic resection.[7] However, the theoretic advantages of the anterior approach over the conventional approach in patients with large HCC have not been documented. In the present study, the surgical and long-term outcomes of hepatic resection for large right-lobe HCC using the anterior approach are compared with the conventional approach.

METHODS

A retrospective study was performed on all patients who underwent major right hepatic resection from January 1989 to December 1997 for HCC 5 cm or more in diameter. Major hepatic resection was defined as resection of three or more liver segments according to the Couinaud nomenclature.[8] The clinical data of all patients were recorded prospectively in a computerized database by a single research assistant. All patients followed the same preoperative evaluation protocol, including blood biochemisty, percutaneous ultrasonography, computed tomography of the abdomen, and in selected patients hepatic and superior mesenteric angiography.[9] Liver function was assessed by both the Child's-Pugh grading[10] and the indocyanine green clearance test, as we reported previously.[11]

Two approaches were adopted for major right hepatic resection for large HCC during the study period. In the conventional approach, the operation started with a bilateral subcostal incision with or without an upward midline extension. Intraoperative ultrasonography was performed routinely to delineate the extent of tumor involvement, to detect tumor nodules in the contralateral lobe and invasion of the tumor into major blood vessels, and to plan and mark the plane of parenchymal transection. Liver hilar dissection was performed and the right hepatic artery and portal vein were controlled. The right lobe of liver, together with the tumor, was then completely mobilized from the posterior abdominal wall and rotated anteriorly and to the left to allow separation of the liver from the inferior vena cava. All the small caval venous branches were individually ligated and divided. The right hepatic vein was then isolated outside the liver, clamped, divided, and sutured. When difficulty was encountered in some patients during mobilization of the right lobe of liver as a result of the huge tumor size, adhesion, or tumor infiltration to the posterior abdominal structures, the abdominal incision was extended into the right thoracic cavity to allow space for the mobilization. Hepatic parenchymal transection was performed after complete control of both the inflow and outflow vessels of the right lobe of liver.

The anterior approach was used in selected patients with large HCC involving the right lobe of liver and infiltrating the posterior abdominal structures or the diaphragm. The decision for anterior approach was entirely determined by the operating surgeon at the time of laparotomy when mobilization of the tumor before parenchymal transection was considered dangerous, difficult, or impossible. After laparotomy through a bilateral subcostal incision and hilar dissection to control the right hepatic artery and portal vein, as in the conventional approach, mobilization of the tumor and the right lobe of liver was not performed. The plane of parenchymal transection, depending on the extent of hepatic resection, was marked on the Glisson capsule with the help of intraoperative ultrasonography. The transection was performed from the anterior surface of the liver down to the right side of liver hilum and down to the anterior surface of the inferior vena cava, which was completely exposed. If concomitant caudate lobectomy was performed, the entire caudate lobe was completely mobilized from the inferior vena cava and retracted toward the right to be resected together with the main specimen. The small caval venous branches were then individually ligated and the right hepatic vein was isolated, clamped, divided, and sutured outside the liver parenchyma. When the specimen was completely disconnected from the inferior vena cava, the right hepatic lobe was mobilized from the right abdominal cavity by dividing the triangular ligament and was delivered (Fig. 1).

All patients received the same postoperative care by the same team of surgeons and were nursed in the intensive care unit during the early postoperative course. Parenteral nutritional support was provided for patients with liver cirrhosis.[12] Early enteric nutrition was encouraged once bowel activity returned. All intraoperative and postoperative complications were recorded prospectively. Hospital death was defined as death during the hospital stay for the hepatic resection. Disease-free survival was calculated from the date of hepatic resection to the date when recurrence was diagnosed.

Statistical analysis was performed by chi-square test or the Fisher exact test to compare discrete variables, and the Mann-Whitney test was used to compare continuous variables. Survival analysis, including cumulative survival and disease-free survival, was estimated by the Kaplan-Meier survival method. Statistical comparison of survival distributions was analyzed by log-rank tests. Multivariate analysis by the Cox proportional hazard regression model was used to identify independent prognostic factors in predicting overall cumulative survival. $P < .05$ was considered to indicate statistical significance. Statistical analyses were performed with SPSS for Windows computer software (SPSS Inc., Chicago, IL).

RESULTS

Of the 330 patients who underwent hepatic resection for HCC between January 1989 and December 1997, 160 underwent major right hepatic resection for tumors larger than 5 cm in diameter. The technique of anterior approach was used in 54 patients (33.8%) and the conventional approach

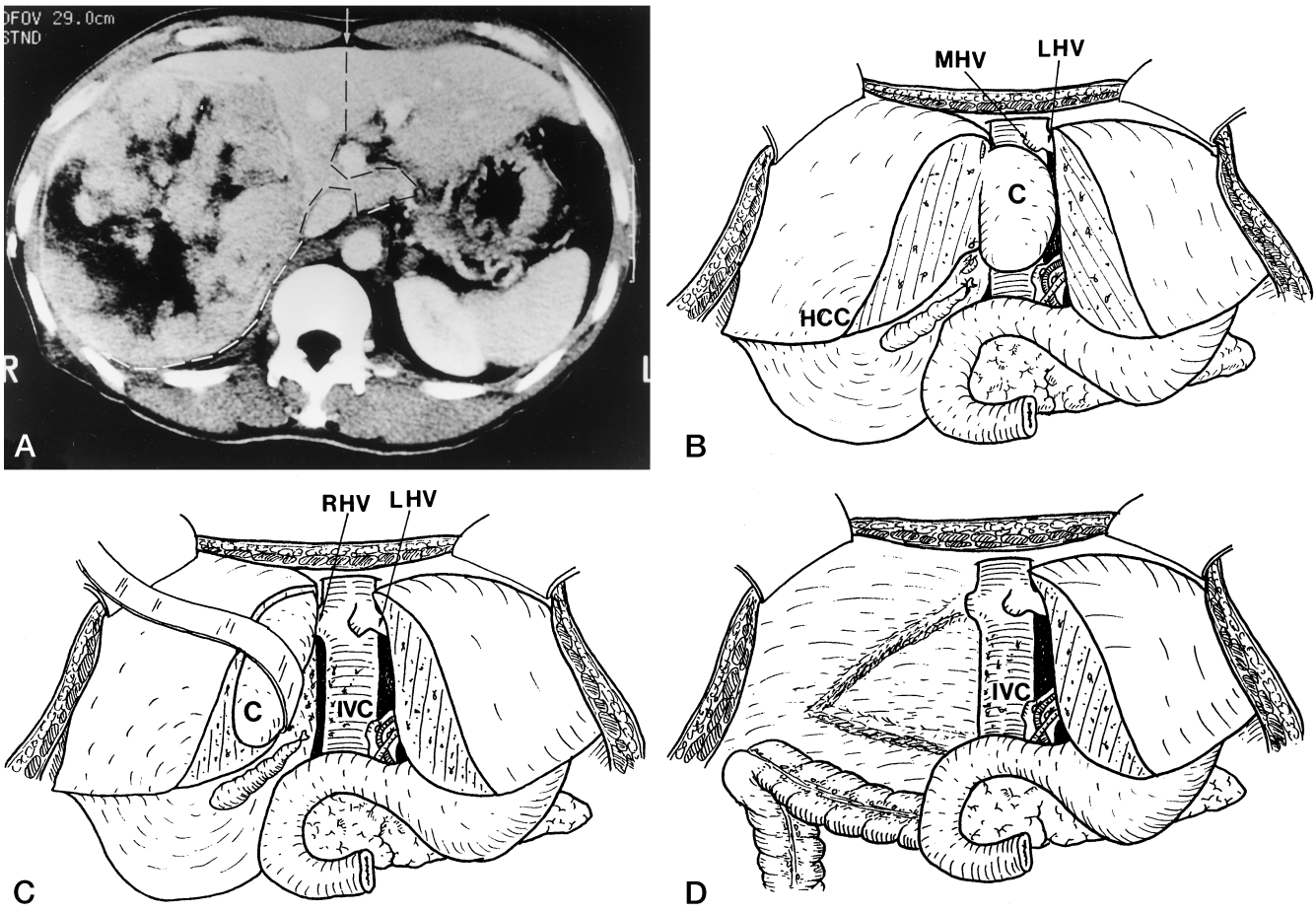

Figure 1. (A) Computed tomography scan showing the direction and line of parenchymal transection in the anterior approach for a large right-lobe hepatocellular carcinoma. (B) Intraoperative diagram of the anterior approach for major right hepatic resection for large hepatocellular carcinoma. Complete hepatic parenchymal transection is performed down to the caudate lobe, and the middle hepatic vein is transected. (C) Intraoperative diagram showing complete transection of hepatic parenchyma and mobilization of the caudate lobe from the inferior vena cava, which is completely exposed. (D) Intraoperative diagram showing completion of hepatic resection and delivery of the specimen. (C, caudate lobe; IVC, inferior vena cava; (LHV, left hepatic vein; MHV, middle hepatic vein; RHV, right hepatic vein)

was used in 106 patients (66.2%). The clinical and laboratory data were comparable in both groups (Table 1), except that there were more men in the conventional approach group. The median size of the tumors was 10.3 cm in the anterior approach group and was comparable to that in the conventional approach group (10.5 cm, $P = .455$). The pathologic data, including tumor-node-metastasis (TNM) staging,[13] were comparable in both groups (Table 2). The extent of hepatic resection in both groups of patients is listed in Table 3. Hepatic resection appeared more extensive in the anterior approach group than in the conventional approach group because concomitant caudate lobe resection was significantly more frequently performed (29.6% vs. 1.9%, $P < .001$). To mobilize the tumor and to control the right hepatic vein before parenchymal resection, thoracotomy was required in 15 patients in the conventional approach group.

The duration of surgery was comparable in the two groups (Table 4). The incidence of intraoperative iatrogenic tumor rupture during mobilization of the right lobe of liver appeared to be higher in the conventional approach group (seven patients, 6.6%) than the anterior approach group (one patient, 1.9 %), although the difference was not significant ($P = .268$). Intraoperative blood loss and blood transfusion requirement were both significantly less and the number of patients without transfusion was also significantly larger in the anterior approach group. The surgical complication rate was comparable in both groups. None of the patients in the anterior approach group died, and all the 14 hospital deaths occurred in the conventional group. The cause of death was liver failure (four patients), intraabdominal sepsis (four patients), chest infection (two patients), heart failure (one patient), intraperitoneal bleeding (one patient), iatrogenic cardiac tamponade from a misplaced central line (one patient), and rapid cancer progression in the liver remnant (one patient).

The median disease-free survival of the anterior approach group was 14.6 months and was significantly better than that

Table 1. CLINICAL AND LABORATORY DATA

Clinical Parameters	Anterior Approach	Conventional Approach	*P*
No. of patients	54	106	—
Male	40 (74.1%)	99 (93.4%)	.001
Age* (yr)	51.5 (18–78)	52 (25–82)	.550
Hepatitis B carrier	46 (85.2%)	90 (84.99%)	.963
Chronic alcoholic	13 (24.1%)	33 (31.1%)	.351
Serum AFP* (ng/mL)	142 (2–1,335,900)	1396 (2–802,900)	.154
Serum albumin* (g/L)	41 (26–52)	42 (31–51)	.158
Serum total bilirubin* (μmol/L)	12 (3–34)	11 (3–63)	.237
AST* (U/L)	50.5 (19–345)	60 (13–804)	.788
Hemoglobin* (g/dL)	13.9 (5–20.2)	13.8 (7.3–21.3)	.333
ICG retention at 15 min* (%)	11.5 (1.6–37.6)	10.9 (1.5–31)	.656

AFP, alpha fetoprotein; AST, aspartate aminotransferase; ICG, indocyanine green.
* Value expressed in median with range in parentheses.

of the conventional approach group (5.6 months, $P = .008$) (Fig. 2). The median overall cumulative survival of the anterior approach group was also significantly better than that of the conventional approach group (59.7 vs. 18.6 months, $P = .016$) (Fig. 3). On follow-up of the 92 patients in the conventional approach group who did not die, pulmonary metastases developed in 41 (44.6%). The incidence was significantly less in the anterior approach group, in which pulmonary metastases developed in 12 (22.2%) of the 54 patients ($P = .007$). At the time of writing, 33 patients remained disease-free with a median follow-up of 73 months: 17 patients (31.5%) were in the anterior approach group and 16 patients (15.1%) were in the conventional group ($P = .015$).

Table 2. PATHOLOGIC DATA

Clinical Parameters	Anterior Approach	Conventional Approach	*P*
Tumor size* (cm)	10.3 (5–25)	10.5 (5–18)	.455
Tumor-free resection margin* (cm)	1 (0–4)	1 (0–5.2)	.505
Resection margin involved by tumor	7 (13.0%)	18 (17.0%)	.508
Venous infiltration of tumor	30 (55.6%)	64 (60.5%)	.558
TNM tumor staging			.056
Stage II	16 (29.6%)	28 (26.4%)	
Stage III	33 (61.1%)	57 (53.8%)	
Stage IVA	2 (3.7%)	19 (17.9%)	
Stage IVB	3 (5.6%)	2 (1.9%)	
Nontumorous liver			.348
Normal	12 (22.2%)	23 (21.7%)	
Chronic hepatitis	27 (50.0%)	42 (39.6%)	
Cirrhosis	15 (27.8%)	41 (38.7%)	

* Value expressed in median with range in parentheses.

Table 3. TYPE OF HEPATIC RESECTION

Hepatic Resection	Anterior Approach	Conventional Approach
Right hepatectomy	24 (44.4%)	67 (63.2%)
Right hepatectomy + caudate lobectomy	9 (16.7%)	1 (0.9%)
Extended right hepatectomy	6 (11.1%)	25 (23.6%)
Extended right hepatectomy + caudate lobectomy	2 (3.7%)	1 (0.9%)
Right lobectomy	8 (14.8%)	12 (11.3%)
Right lobectomy + caudate lobectomy	5 (9.3%)	0 (0%)
Total	**54 (100%)**	**106 (100%)**

Variables that might affect overall cumulative survival of the entire patient population in this study (i.e., tumor size, TNM stage, blood loss volume, blood transfusion, venous invasion in the HCC, and use of anterior approach) were subjected to Cox regression analysis. The TNM stage, use of anterior approach, tumor size, and intraoperative blood loss volume were found to be independent factors influencing the overall cumulative survival (Table 5).

DISCUSSION

Despite recent reports on the satisfactory outcome of hepatectomy for HCC,[14–16] major right hepatic resection for large HCC remains a major surgical challenge, especially when underlying liver cirrhosis is present.[17–20] With the conventional approach, complications may arise during difficult mobilization of the right lobe of liver, leading to

Table 4. INTRAOPERATIVE AND POSTOPERATIVE DATA

Intraoperative and Postoperative Data	Anterior Approach	Conventional Approach	*P*
Intraoperative blood loss* (L)	2.0 (0.6–20)	2.5 (0.2–20)	.044
Intraoperative blood transfusion* (L)	0.52 (0–12.9)	1.5 (0–9.6)	.001
No. of patients without transfusion	23 (42.6%)	20 (18.9%)	.001
Operating time* (min)	395 (210–780)	375 (210–675)	.144
Bile duct injury	1 (1.9%)	2 (1.9%)	1.0
Intraoperative tumor rupture	1 (1.9%)	7 (6.6%)	.268
ICG retention at 15 min* (%), on postoperative day 7	20 (6.7–66.5)	19.7 (4–61.5)	.475
Surgical complications	23 (42.6%)	47 (44.3%)	.833
Hospital deaths	0 (0%)	14 (13.2%)	.003
Median disease-free survival (months)	14.6	5.6	.008
Median survival (months)	59.7	18.6	.016

ICG, indocyanine green.
* Value expressed in median with range in parentheses.

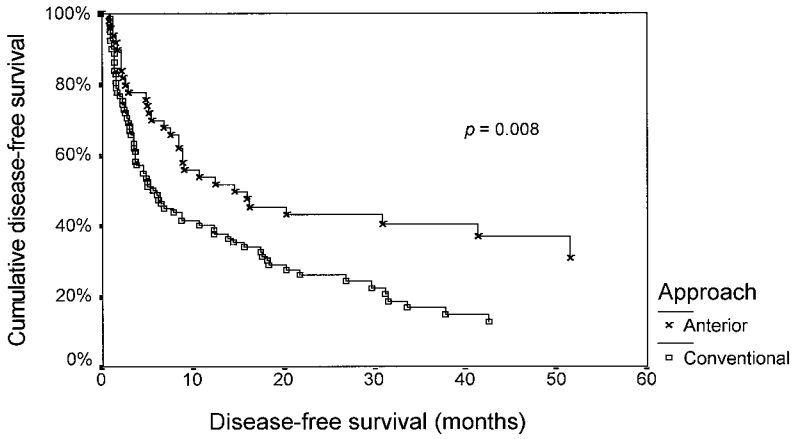

Figure 2. Disease-free survival of patients who underwent major right hepatic resection using the anterior approach (54 patients) and the conventional approach (106 patients).

unfavorable surgical outcomes. The anterior approach was first described by Ozawa[21] as one of the "nonconventional approaches" to advanced liver cancer in an attempt to avoid prolonged rotation and displacement of the hepatic lobes, causing impairment of the afferent and efferent circulation. In the current report, the technique of anterior approach was shown to result in favorable surgical and long-term survival outcomes of the patients who underwent major right hepatic resection for large HCC compared with those using the conventional approach. The better outcome might be related to the reduction in blood loss, because excessive intraoperative bleeding has been reported to have a detrimental effect on the postoperative liver function and to result in an increased perioperative death rate.[22,23] Perioperative transfusion has also been found to promote recurrence of HCC after hepatic resection, resulting in short disease-free and overall survivals.[24,25]

HCC is well known to be a soft, friable, and highly vascular tumor. Forceful retraction of large right-lobe HCC during difficult mobilization using the conventional approach can result in rupture of the tumor. This usually leads to excessive bleeding and tumor cell spillage into the peritoneal cavity. As a reaction to the ongoing bleeding from intraoperative tumor rupture, the hepatic resection is usually performed in a hurry and may lead to further excessive bleeding. However, when the anterior approach is used, the right lobe of the liver, together with the tumor, is completely separated from the inferior vena cava before mobilization. Therefore, mobilization can be performed from all directions, including the medial aspect. Mobilization of the tumor from retroperitoneal adhesion or infiltration, if present, can then be performed quickly. Resection of adjacent structures, including the diaphragm or the right adrenal gland, can also be performed at this stage if necessary.

Hematogenous dissemination of malignant tumor cells has been reported during surgical resection of biliary-pancreatic cancer,[26,27] colorectal cancer[28] and prostatic cancer.[29] It was considered related to manipulation of the tumors during surgery, and the "no-touch" isolation technique has been reported to reduce intraoperative shedding of tumor cells into the portal vein during resection of colorectal cancer.[30] In patients with HCC, venous permeation or vascular invasion of the tumor is common.[31,32] This phenomenon may be responsible for the high incidence of hematogenous spread before resection, but compression of the tumor during mobilization may enhance the spread of tumor cells into the systemic circulation[33,34] or the intrahepatic portal venous system.[35] The potential risk of tumor

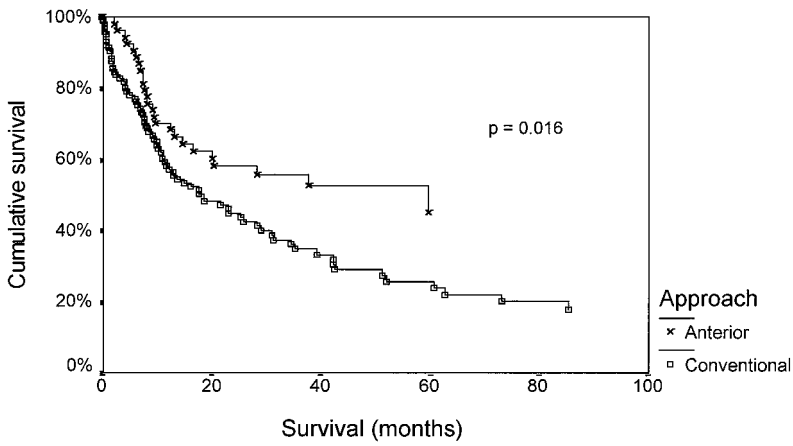

Figure 3. Cumulative overall survival of patients who underwent major right hepatic resection using the anterior approach (54 patients) and the conventional approach (106 patients).

Table 5. FACTORS AFFECTING OVERALL CUMULATIVE SURVIVAL

Independent Factor	Relative Risk	95% Confidence Interval
TNM tumor staging	1.4874	1.1008–2.0098
Anterior approach	1.2885	1.0119–1.6407
Tumor size	1.0742	1.0157–1.1361
Intraoperative blood loss	1.0724	1.0150–1.1331

Multivariate analysis of all patients undergoing major right hepatic resection; Cox regression analysis.

cell dissemination can theoretically be minimized with use of the anterior approach. However, in this retrospective study, we did not assess the presence of cancer cells in the circulation, such as positive reverse transcription polymerase chain reaction alpha fetoprotein mRNA. Such evidence should be evaluated in a prospective randomized trial.

Another deficiency of the present retrospective study is the fact that there were more patients with TNM stage IVA disease in the conventional approach group. TNM stage was shown to be a major determinant of long-term survival of HCC after hepatectomy.[36,37] To define the role of the anterior approach, multivariate analysis was performed, and the anterior approach was found to be one of the independently significant factors affecting long-term survival. Comparison of survival according to tumor stage was not performed in this study because the numbers in each subgroup were relatively small and uneven in distribution. In the future prospective randomized trial, randomization by stratification according to TNM stage should be performed to validate that anterior approach does improve the result of hepatectomy in all TNM stages of HCC.

The duration of surgery was comparable in both groups of patients, although more patients in the anterior approach group had concomitant caudate lobe resection. In the anterior approach group, to avoid hepatic vein injury resulting in excessive bleeding, extreme care had to be taken during parenchymal transection using the ultrasonic dissector. This often resulted in prolonged transection time. In the conventional approach group, however, more time was spent in hemostasis and difficult mobilization of the tumor before parenchymal transection, which sometimes required thoracotomy for adequate exposure.

Despite its advantages over the conventional approach, the anterior approach is potentially dangerous. Torrential bleeding can occur at the deeper plane of parenchymal transection (e.g., from the middle hepatic vein) and can be difficult to control. Without prior mobilization of the right lobe of liver and the tumor, the hepatic lobe cannot be lifted up and compressed manually for hemostasis or rapid transection. Therefore, we had previously recommended that this approach should be reserved for tumor invading the hepatic vein.[9] Given the results of the present study, our view is modified. The anterior approach might be the preferred technique if adequate experience in liver transection has been accumulated, parenchymal transection is performed with extreme care, and venous bleeding is controlled promptly with fine sutures.

In conclusion, the anterior approach was the preferred technique for major right hepatic resection for large HCC because it resulted in improved surgical and survival outcomes. Further studies are required to document the advantages of the anterior approach as a routine technique for all right hepatic resections for HCC and other hepatic tumors, ideally in a prospective randomized trial.

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